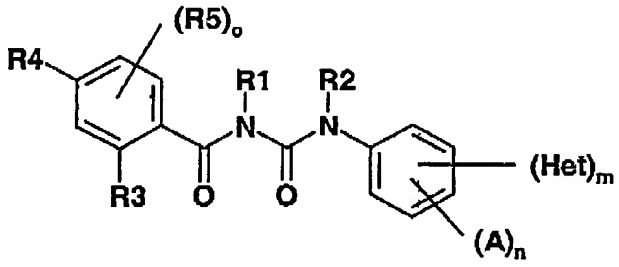
DEAV2002/0050 US NP

We claim:

1. (currently amended) A compound of the formula I,




I

wherein

R1 and R2 are each independently H, O-($C_1$-$C_6$)-alkyl, CO-($C_1$-$C_6$)-alkyl, COO-($C_1$-$C_6$)-alkyl, ($C_1$-$C_6$)-alkylene-COOH, ($C_1$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl or ($C_1$-$C_6$)-alkyl, wherein said ($C_1$-$C_6$)-alkyl is optionally substituted by OH, O-($C_1$-$C_4$)-alkyl, $NH_2$, NH($C_1$-$C_4$)-alkyl or N[($C_1$-$C_6$)-alkyl]$_2$;

R3 and R4 are each independently F, Cl, Br, OH, $NO_2$, CN, ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, O-($C_2$-$C_6$)-alkenyl or ($C_2$-$C_6$)-alkynyl, wherein said ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, O-($C_2$-$C_6$)-alkenyl and ($C_2$-$C_6$)-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

R5 is H, F, Cl, Br, OH, $NO_2$, CN, ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_0$-$C_6$)-alkylene-COOH, ($C_0$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl, O-($C_2$-$C_6$)-alkenyl or ($C_2$-$C_6$)-alkynyl, wherein said ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_0$-$C_6$)-alkylene-COOH, ($C_0$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl, O-($C_2$-$C_6$)-alkenyl and ($C_2$-$C_6$)-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

A is H, F, Cl, Br, OH, $NO_2$, CN, $(C_1-C_6)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-COOH, $(C_1-C_6)$-alkylene-COO$(C_1-C_6)$-alkyl, $SO_2$-$(C_1-C_6)$-alkyl, $(C_2-C_6)$-alkenyl, $(C_2-C_6)$-alkynyl, O-$(C_1-C_6)$-alkyl, $S(O)_{1-2}$-$(C_1-C_6)$-alkyl-, NH-$(C_1-C_6)$-alkyl, N-$[(C_1-C_6)$-alkyl$]_2$, COO-$(C_1-C_6)$-alkyl, $CONH_2$, CONH-$(C_1-C_6)$-alkyl, CON-$[(C_1-C_6)$-alkyl$]_2$, $SO_2NH_2$, $SO_2$NH-$(C_1-C_6)$-alkyl, $SO_2$N-$[(C_1-C_6)$-alkyl$]_2$ or NHCOR6, wherein said $(C_1-C_6)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-COOH, $(C_1-C_6)$-alkylene-COO$(C_1-C_6)$-alkyl, $SO_2$-$(C_1-C_6)$-alkyl, $(C_2-C_6)$-alkenyl, $(C_2-C_6)$-alkynyl, O-$(C_1-C_6)$-alkyl, $S(O)_{1-2}$-$(C_1-C_6)$-alkyl-, NH-$(C_1-C_6)$-alkyl, N-$[(C_1-C_6)$-alkyl$]_2$, COO-$(C_1-C_6)$-alkyl, CONH-$(C_1-C_6)$-alkyl, CON-$[(C_1-C_6)$-alkyl$]_2$, $SO_2$NH-$(C_1-C_6)$-alkyl and $SO_2$N-$[(C_1-C_6)$-alkyl$]_2$ are optionally mono- or polysubstituted by F, Cl, Br, COOH, COO-$(C_1-C_6)$-alkyl, $CONH_2$, CONH-$(C_1-C_6)$-alkyl, CON$[(C_1-C_6)$-alkyl$]_2$ or OCO-$(C_1-C_6)$-alkyl;

R6 is H, $(C_1-C_6)$-alkyl, $(C_3-C_7)$-cycloalkyl, $(C_3-C_7)$-cycloalkyl-$(C_1-C_4)$-alkylene, $(C_2-C_6)$-alkenyl, $(C_2-C_6)$-alkynyl, $(C_1-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-CO-$(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-COOH, $(C_1-C_6)$-alkylene-$CONH_2$, $(C_6-C_{10})$-aryl, $(C_1-C_4)$-alkylene-$(C_6-C_{10})$-aryl, heteroaryl, $(C_1-C_4)$-alkylene-heteroaryl or CO-heteroaryl, wherein said $(C_1-C_6)$-alkyl, $(C_3-C_7)$-cycloalkyl, $(C_3-C_7)$-cycloalkyl-$(C_1-C_4)$-alkylene, $(C_2-C_6)$-alkenyl, $(C_2-C_6)$-alkynyl, $(C_1-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-CO-$(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-COOH and $(C_1-C_6)$-alkylene-$CONH_2$ are optionally mono- or polysubstituted by F, Cl, Br, O$(C_1-C_4$-alkyl), COO-$(C_1-C_4$-alkyl) or N-$[(C_1-C_4)$-alkyl$]_2$ and said $(C_6-C_{10})$-aryl, $(C_1-C_4)$-alkylene-$(C_6-C_{10})$-aryl, heteroaryl, $(C_1-C_4)$-alkylene-heteroaryl and CO-heteroaryl are optionally mono- or polysubstituted by F, Cl, Br, $NO_2$, CN, O-$(C_1-C_4$-alkyl), S-COO$(C_1-C_4$-alkyl), COO-$(C_1-C_4$-alkyl), N-$[(C_1-C_4)$-alkyl$]_2$ or $(C_1-C_6)$-alkyl;

n is 0, 1, 2 or 3;

m is 1, 2, 3, 4 or 5;

o is 0, 1, 2 or 3;

Het is a heterocyclic 4- to 7-membered ring which may contain up to four N, O or S heteroatoms and wherein said heterocyclic 4- to 7-membered ring is optionally substituted by R7, R8 and R9, with the proviso that said heterocyclic 4- to 7- membered ring cannot be pyrrole; and

R7, R8, and R9 are each independently H, F, Cl, Br, $(C_1-C_6)$-alkyl, O-$(C_1-C_6)$-alkyl, O-$(C_2-C_6)$-alkenyl, O-$(C_2-C_6)$-alkynyl, OH, oxo, O-$(C_1-C_6)$-alkyl, $NH_2$, NH-$(C_1-C_6)$-alkyl, N-$[(C_1-C_6)$-alkyl$]_2$, COOH, CO-$(C_1-C_6)$-alkyl, COO-$(C_1-C_6)$-alkyl, $CONH_2$, CONH-$(C_1-C_6)$-alkyl, CON-$[(C_1-C_6)$-alkyl$]_2$, $(C_0-C_6)$-alkylene-aryl or $(C_1-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, wherein said $(C_1-C_6)$-alkyl, O-$(C_1-C_6)$-alkyl, O-$(C_2-C_6)$-alkenyl, O-$(C_2-C_6)$-alkynyl, O-$(C_1-C_6)$-alkyl, NH-$(C_1-C_6)$-alkyl, N-$[(C_1-C_6)$-alkyl$]_2$, CO-$(C_1-C_6)$-alkyl, COO-$(C_1-C_6)$-alkyl, CONH-$(C_1-C_6)$-alkyl, CON-$[(C_1-C_6)$-alkyl$]_2$, $(C_0-C_6)$-alkylene-aryl and $(C_1-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl are optionally substituted by COOH, $CONH_2$, CONH-$(C_1-C_6)$-alkyl, CON-$[(C_1-C_6)$-alkyl$]_2$, OCO-$(C_1-C_6)$-alkyl, F, Cl, $(C_1-C_6)$-alkyl or O-$(C_1-C_6)$-alkyl; and two radicals selected from said R7, R8 and R9 may optionally be bonded together to form a ring fused onto said heterocyclic 4- to 7-membered ring;

and pharmaceutically acceptable salts thereof.

2. (currently amended) The compound of Claim 1 wherein

R1 and R2 are H;

R3 and R4 are each independently F, Cl or Br;

R5 is H, F, Cl, Br, OH, $NO_2$, CN, $(C_1-C_6)$-alkyl, O-$(C_1-C_4)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-COOH; $(C_0-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, $SO_2$-$(C_1-C_6)$-alkyl, O-$(C_2-C_6)$-alkenyl or $(C_2-C_6)$-alkynyl, wherein said $(C_1-C_6)$-alkyl, O-$(C_1-C_4)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-COOH, $(C_0-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, $SO_2$-$(C_1-C_6)$-alkyl, O-$(C_2-C_6)$-alkenyl and $(C_2-C_6)$-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

A is H, F, Cl, Br, OH, $NO_2$, CN, $(C_1-C_6)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-COOH, $(C_1-C_6)$-alkylene-COO$(C_1-C_6)$-alkyl, $SO_2$-$(C_1-C_6)$-alkyl, $(C_2-C_6)$-alkenyl, $(C_2-C_6)$-alkynyl, O-$(C_1-C_6)$-alkyl, $S(O)_{1-2}$-$(C_1-C_6)$-alkyl-, NH-$(C_1-C_6)$-alkyl, N-$[(C_1-C_6)$-alkyl$]_2$, COO-$(C_1-C_6)$-alkyl, $CONH_2$, CONH-$(C_1-C_6)$-alkyl, CON-$[(C_1-C_6)$- alkyl$]_2$, $SO_2NH_2$, $SO_2$NH-$(C_1-C_6)$-alkyl, $SO_2$N-$[(C_1-C_6)$-alkyl$]_2$ or NHCOR6, wherein said $(C_1-C_6)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-COOH, $(C_1-C_6)$-alkylene-COO$(C_1-C_6)$-alkyl, $SO_2$-$(C_1-C_6)$-alkyl, $(C_2-C_6)$-alkenyl, $(C_2-C_6)$-alkynyl, O-$(C_1-C_6)$-alkyl, $S(O)_{1-2}$-$(C_1-C_6)$-alkyl-, NH-$(C_1-C_6)$-alkyl, N-$[(C_1-C_6)$-alkyl$]_2$, COO-$(C_1-C_6)$-alkyl, CONH-$(C_1-C_6)$-alkyl, CON-$[(C_1-C_6)$- alkyl$]_2$, $SO_2$NH-$(C_1-C_6)$-alkyl and $SO_2$N-$[(C_1-C_6)$-alkyl$]_2$ are optionally mono- or polysubstituted by F, Cl, Br, COOH, COO-$(C_1-C_6)$-alkyl, $CONH_2$, CONH-$(C_1-C_6)$-alkyl, CON-$[(C_1-C_6)$-alkyl$]_2$ or OCO-$(C_1-C_6)$-alkyl;

R6 is H, $(C_1-C_6)$-alkyl, $(C_3-C_7)$-cycloalkyl, $(C_3-C_7)$-cycloalkyl-$(C_1-C_4)$-alkylene, $(C_2-C_6)$-alkenyl, $(C_2-C_6)$-alkynyl, $(C_1-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-CO-$(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-COOH, $(C_1-C_6)$-alkylene-$CONH_2$, $(C_6-C_{10})$-aryl, $(C_1-C_4)$-alkylene-$(C_6-C_{10})$-aryl, heteroaryl, $(C_1-C_4)$-alkylene-heteroaryl or CO-heteroaryl, wherein said $(C_1-C_6)$-alkyl, $(C_3-C_7)$-cycloalkyl, $(C_3-C_7)$-cycloalkyl-$(C_1-C_4)$-alkylene, $(C_2-C_6)$-alkenyl, $(C_2-C_6)$-alkynyl, $(C_1-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-CO-$(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-COOH and $(C_1-C_6)$-

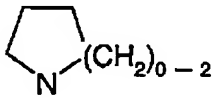
alkylene-$CONH_2$ are optionally mono- or polysubstituted by F, Cl, Br, O-$(C_1$-$C_4)$-alkyl, COO-$(C_1$-$C_4$-alkyl), or N-$[(C_1$-$C_4)$-alkyl$]_2$, and said $(C_6$-$C_{10})$-aryl, $(C_1$-$C_4)$-alkylene-$(C_6$-$C_{10})$-aryl, heteroaryl, $(C_1$-$C_4)$-alkylene-heteroaryl and CO-heteroaryl are optionally mono- or polysubstituted by F, Cl, Br, $NO_2$, CN, O-$(C_1$-$C_4$-alkyl), COO-$(C_1$-$C_4$-alkyl), S-COO$(C_1$-$C_4$-alkyl), N-$[(C_1$-$C_4)$-alkyl$]_2$ or $(C_1$-$C_6)$-alkyl;

n is 0, 1 or 2;

m is 1;

o is 0 or 1;

Het is a heterocyclic 4- to 7-membered ring selected from triazolyl, tetrazolyl, oxadiazolyl, pyrazolyl, benzimidazolyl, furyl, triazinyl or



wherein said heterocyclic 4- to 7-membered ring is optionally substituted by R7, R8 and R9; and

R7, R8, and R9 are each independently H, F, Cl, Br, $(C_1$-$C_6)$-alkyl , O-$(C_1$-$C_6)$-alkyl, O-$(C_2$-$C_6)$-alkenyl, O-$(C_2$-$C_6)$-alkynyl, OH, oxo, O-$(C_1$-$C_6)$-alkyl, $NH_2$, NH-$(C_1$-$C_6)$-alkyl, N-$[(C_1$-$C_6)$-alkyl$]_2$, COOH, CO-$(C_1$-$C_6)$-alkyl, COO-$(C_1$-$C_6)$-alkyl, $CONH_2$, CONH-$(C_1$-$C_6)$-alkyl, CON-$[(C_1$-$C_6)$-alkyl$]_2$, $(C_0$-$C_6)$-alkylene-aryl or $(C_1$-$C_6)$-alkylene-COO-$(C_1$-$C_6)$-alkyl, wherein said $(C_1$-$C_6)$-alkyl , O-$(C_1$-$C_6)$-alkyl, O-$(C_2$-$C_6)$-alkenyl, O-$(C_2$-$C_6)$-alkynyl, O-$(C_1$-$C_6)$-alkyl, NH-$(C_1$-$C_6)$-alkyl, N-$[(C_1$-$C_6)$-alkyl$]_2$, CO-$(C_1$-$C_6)$-alkyl, COO-$(C_1$-$C_6)$-alkyl, CONH-$(C_1$-$C_6)$-alkyl, CON-$[(C_1$-$C_6)$-alkyl$]_2$, $(C_0$-$C_6)$-alkylene-aryl and $(C_1$-$C_6)$-alkylene-COO-$(C_1$-$C_6)$-alkyl are optionally substituted by COOH, $CONH_2$, CONH-$(C_1$-$C_6)$-alkyl, CON-$[(C_1$-$C_6)$-alkyl$]_2$, OCO-$(C_1$-$C_6)$-alkyl, F, Cl, $(C_1$-$C_6)$-alkyl or O-$(C_1$-$C_6)$-alkyl;

and two radicals selected from said R7, R8 and R9 may optionally be bonded together to form a ring fused onto said heterocyclic 4- to 7-membered ring;

and pharmaceutically acceptable salts thereof.

3. (currently amended) The compound of Claim 2 wherein

R1 and R2 are H;

R3 and R4 are each independently F, Cl or Br;

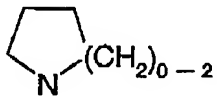
R5 is H, F, Cl, Br, OH, $NO_2$, CN, $(C_1-C_6)$-alkyl, O-$(C_1-C_4)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-COOH, $(C_0-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, $SO_2$-$(C_1-C_6)$-alkyl, O-$(C_2-C_6)$-alkenyl or $(C_2-C_6)$-alkynyl, wherein said $(C_1-C_6)$-alkyl, O-$(C_1-C_4)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-COOH, $(C_0-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, $SO_2$-$(C_1-C_6)$-alkyl, O-$(C_2-C_6)$-alkenyl and $(C_2-C_6)$-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

A is H, F, Cl, Br, $(C_1-C_6)$-alkyl, $CF_3$, $OCF_3$, $NO_2$, CN, O-$(C_1-C_6)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-COOH, $(C_1-C_6)$-alkylene-COO-$(C_1-C_6)$-alkyl, COO-$(C_1-C_6)$-alkyl or $SO_2$-$(C_1-C_6)$-alkyl;

n is 0, 1 or 2;

m is 1;

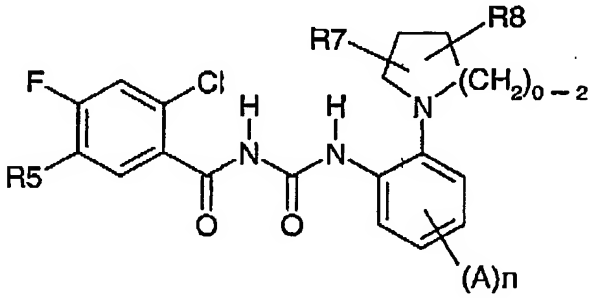
o is 0 or 1;

Het is a heterocyclic 4- to 7-membered ring group selected from triazolyl, tetrazolyl, oxadiazolyl, furyl, triazinyl or  , wherein said 4- to 7-membered heterocyclic ring is optionally substituted by R7, R8 and R9; and

R7, R8, and R9 are each independently H, ($C_1$-$C_6$)-alkyl, OH, oxo, $NH_2$, COOH, COO-($C_1$-$C_6$)-alkyl, $CONH_2$, CONH-($C_1$-$C_6$)-alkyl or CON-[($C_1$-$C_6$)-alkyl]$_2$, wherein said ($C_1$-$C_6$)-alkyl, COO-($C_1$-$C_6$)-alkyl, CONH-($C_1$-$C_6$)-alkyl and CON-[($C_1$-$C_6$)-alkyl]$_2$ are optionally substituted by COOH;

and pharmaceutically acceptable salts thereof.

4. (currently amended) The compound of Claim 1 wherein the compound has the structure Ia



Ia

wherein

R5 is H, F, Cl, Br, ($C_1$-$C_6$)-alkyl, $CF_3$, $OCF_3$, $NO_2$, CN, O-($C_1$-$C_6$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_0$-$C_6$)-alkylene-COOH, ($C_0$-$C_6$)-alkylene–COO-($C_1$-$C_6$)-alkyl or $SO_2$-($C_1$-$C_6$)-alkyl;

A is H, F, Cl, Br, $(C_1-C_6)$-alkyl, $CF_3$, $OCF_3$, $NO_2$, CN, O-$(C_1-C_6)$-alkyl, CO-$(C_1-C_6)$-alkyl, $(C_1-C_6)$-alkylene-COOH, $(C_1-C_6)$-alkylene–COO-$(C_1-C_6)$-alkyl, COO-$(C_1-C_6)$-alkyl or $SO_2$-$(C_1-C_6)$-alkyl;

R7 is H, $(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-aryl, O-$(C_1-C_6)$-alkyl, O-$(C_2-C_6)$-alkenyl or O-$(C_2-C_6)$-alkynyl, wherein said $(C_1-C_6)$-alkyl, $(C_0-C_6)$-alkylene-aryl, O-$(C_1-C_6)$-alkyl, O-$(C_2-C_6)$-alkenyl and O-$(C_2-C_6)$-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

R8 is -(C=O)-X;

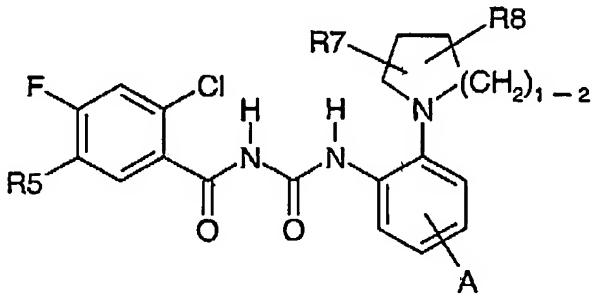
X is OH, O-$(C_1-C_6)$-alkyl, $NH_2$, NH-$(C_1-C_6)$-alkyl or N-$((C_1-C_6)$-alkyl$)_2$;

m is 1 or 2; and

n is 1 or 2;

and pharmaceutically acceptable salts thereof.

5. (previously amended) The compound of Claim 1 wherein the compound has the structure Iaa




Iaa

wherein

R5 is H or F;

A is H, F, Cl, $(C_1-C_6)$-alkyl, $CF_3$, $COO-(C_1-C_6)$-alkyl, or $SO_2-(C_1-C_6)$-alkyl;

R7 is H or phenyl;

R8 is -(C=O)-X; and

X is OH, $O-(C_1-C_6)$-alkyl, $NH_2$, $NH-(C_1-C_6)$-alkyl or $N-[(C_1-C_6)-alkyl]_2$;

and pharmaceutically acceptable salts thereof.

6. (original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and one or more compounds of Claim 1.

7. (previously amended) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and one or more compounds of Claim 1 and at least one further active ingredient.

8. (withdrawn) The pharmaceutical composition of Claim 7, wherein said further active ingredient is selected from the group consisting of:
antidiabetics, hypoglycemic active ingredients, HMG-CoA reductase inhibitors, cholesterol absorption inhibitors, PPAR gamma agonists, PPAR alpha agonists, PPAR alpha/gamma agonists, fibrates, MTP inhibitors, bile acid absorption inhibitors, CETP inhibitors, polymeric bile acid adsorbents, LDL receptor inducers, ACAT inhibitors, antioxidants, lipoprotein lipase inhibitors, ATP-citrate-lyase inhibitors, squalene synthetase inhibitors, lipoprotein(a) antagonists, lipase inhibitors, insulins, sulfonylureas, biguanides, meglitinides, thiazolidinediones, α-glucosidase inhibitors, active ingredients acting on the ATP-dependent potassium channel of the beta cells, CART agonists, NPY

agonists, MC4 agonists, orexin agonists, H3 agonists, TNF agonists, CRF agonists, CRF BP antagonists, urocortin agonists, β3 agonists, MSH (melanocyte-stimulating hormone) agonists, CCK agonists, serotonin reuptake inhibitors, mixed serotoninergic and noradrenergic compounds, 5HT agonists, bombesin agonists, galanin antagonists, growth hormones, growth hormone-releasing compounds, TRH agonists, uncoupling protein 2 or 3 modulators, leptin agonists, DA agonists (bromocriptine, Doprexin), lipase/amylase inhibitors, PPAR modulators, RXR modulators or TR-β agonists or amphetamines.

9. (original) A method of reducing blood sugar comprising administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1.

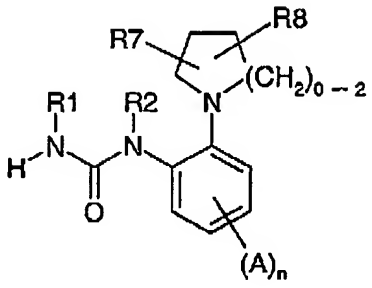
10. (original) A method for treating lipid and carbohydrate metabolism disorders comprising administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1.

11. (original) A method for treating type 2 diabetes comprising administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1.

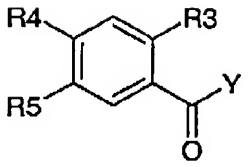
12. (original) A method for treating arteriosclerotic symptoms comprising administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1.

13. (original) A method for treating insulin resistance comprising administering to a patient in need thereof a therapeutically effective amount of a compound of Claim 1.

14. (currently amended) A process for preparing a compound of Claim 1, which comprises reacting a urea of formula 2 with a compound of formula 4




2




4

wherein

R1 and R2 are each independently H, O-($C_1$-$C_6$)-alkyl, CO-($C_1$-$C_6$)-alkyl, COO-($C_1$-$C_6$)-alkyl, ($C_1$-$C_6$)-alkylene-COOH, ($C_1$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl or ($C_1$-$C_6$)-alkyl, wherein said ($C_1$-$C_6$)-alkyl is optionally substituted by OH, O-($C_1$-$C_4$)-alkyl, $NH_2$, NH($C_1$-$C_4$)-alkyl or N[($C_1$-$C_6$)-alkyl]$_2$;

R3 and R4 are each independently F, Cl, Br, OH, $NO_2$, CN, ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, O-($C_2$-$C_6$)-alkenyl or ($C_2$-$C_6$)-alkynyl, wherein said ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, O-($C_2$-$C_6$)-alkenyl and ($C_2$-$C_6$)-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

R5 is H, F, Cl, Br, OH, $NO_2$, CN, ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_0$-$C_6$)-alkylene-COOH, ($C_0$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl, O-($C_2$-$C_6$)-alkenyl or ($C_2$-$C_6$)-alkynyl, wherein said ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_0$-$C_6$)-alkylene-COOH, ($C_0$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl, O-($C_2$-$C_6$)-alkenyl and ($C_2$-$C_6$)-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

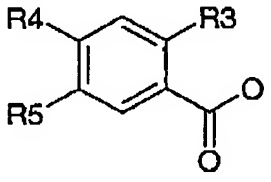
A is H, F, Cl, Br, OH, $NO_2$, CN, ($C_1$-$C_6$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_1$-$C_6$)-alkylene-COOH, ($C_1$-$C_6$)-alkylene-COO($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl, ($C_2$-$C_6$)-alkenyl, ($C_2$-$C_6$)-alkynyl, O-($C_1$-$C_6$)-alkyl, S(O)$_{1-2}$-($C_1$-$C_6$)-alkyl-, NH-($C_1$-$C_6$)-alkyl, N-[($C_1$-$C_6$)-alkyl]$_2$, COO-($C_1$-$C_6$)-alkyl, $CONH_2$, CONH-($C_1$-$C_6$)-alkyl, CON-[($C_1$-$C_6$)-alkyl]$_2$, $SO_2NH_2$, $SO_2$NH-($C_1$-$C_6$)-

alkyl, $SO_2N$-[($C_1$-$C_6$)-alkyl]$_2$ or NHCOR6, wherein said ($C_1$-$C_6$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_1$-$C_6$)-alkylene-COOH; ($C_1$-$C_6$)-alkylene-COO($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl, ($C_2$-$C_6$)-alkenyl, ($C_2$-$C_6$)-alkynyl, O-($C_1$-$C_6$)-alkyl, $S(O)_{1-2}$-($C_1$-$C_6$)-alkyl-, NH-($C_1$-$C_6$)-alkyl, N-[($C_1$-$C_6$)-alkyl]$_2$, COO-($C_1$-$C_6$)-alkyl, CONH-($C_1$-$C_6$)-alkyl, CON-[($C_1$-$C_6$)-alkyl]$_2$, $SO_2$NH-($C_1$-$C_6$)-alkyl and $SO_2N$-[($C_1$-$C_6$)-alkyl]$_2$ are optionally mono- or polysubstituted by F, Cl, Br, COOH, COO-($C_1$-$C_6$)-alkyl, $CONH_2$, CONH-($C_1$-$C_6$)-alkyl, CON[($C_1$-$C_6$)-alkyl]$_2$ or OCO-($C_1$-$C_6$)-alkyl;

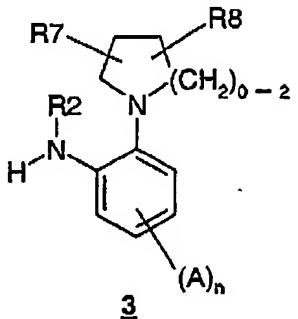
n is 0, 1, 2 or 3;

R7 and R8 are each independently H, F, Cl, Br, ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_6$)-alkyl, O-($C_2$-$C_6$)-alkenyl, O-($C_2$-$C_6$)-alkynyl, OH, oxo, O-($C_1$-$C_6$)-alkyl, $NH_2$, NH-($C_1$-$C_6$)-alkyl, N-[($C_1$-$C_6$)-alkyl]$_2$, COOH, CO-($C_1$-$C_6$)-alkyl, COO-($C_1$-$C_6$)-alkyl, $CONH_2$, CONH-($C_1$-$C_6$)-alkyl, CON-[($C_1$-$C_6$)-alkyl]$_2$, ($C_0$-$C_6$)-alkylene-aryl or ($C_1$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl, wherein said ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_6$)-alkyl, O-($C_2$-$C_6$)-alkenyl, O-($C_2$-$C_6$)-alkynyl, O-($C_1$-$C_6$)-alkyl, NH-($C_1$-$C_6$)-alkyl, N-[($C_1$-$C_6$)-alkyl]$_2$, CO-($C_1$-$C_6$)-alkyl, COO-($C_1$-$C_6$)-alkyl, CONH-($C_1$-$C_6$)-alkyl, CON-[($C_1$-$C_6$)-alkyl]$_2$, ($C_0$-$C_6$)-alkylene-aryl and ($C_1$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl are optionally substituted by COOH, $CONH_2$, CONH-($C_1$-$C_6$)-alkyl, CON-[($C_1$-$C_6$)-alkyl]$_2$, OCO-($C_1$-$C_6$)-alkyl, F, Cl, ($C_1$-$C_6$)-alkyl or O-($C_1$-$C_6$)-alkyl; and said R7 and R8 may optionally be bonded together to form a ring fused onto said heterocyclic 4- to 7-membered ring; and

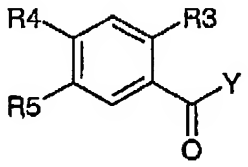
Y is Cl or



15. (currently amended) A process for preparing a compound of Claim 1, which comprises reacting an aniline derivative of formula 3 with a compound of formula 4




3




4

wherein

R2 is H, O-($C_1$-$C_6$)-alkyl, CO-($C_1$-$C_6$)-alkyl, COO-($C_1$-$C_6$)-alkyl, ($C_1$-$C_6$)-alkylene-COOH, ($C_1$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl or ($C_1$-$C_6$)-alkyl, wherein said ($C_1$-$C_6$)-alkyl is optionally substituted by OH, O-($C_1$-$C_4$)-alkyl, $NH_2$, NH($C_1$-$C_4$)-alkyl or N[($C_1$-$C_6$)-alkyl]$_2$;

R3 and R4 are each independently F, Cl, Br, OH, $NO_2$, CN, ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, O-($C_2$-$C_6$)-alkenyl or ($C_2$-$C_6$)-alkynyl, wherein said ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, O-($C_2$-$C_6$)-alkenyl and ($C_2$-$C_6$)-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

R5 is H, F, Cl, Br, OH, $NO_2$, CN, ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_0$-$C_6$)-alkylene-COOH, ($C_0$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl, O-($C_2$-$C_6$)-alkenyl or ($C_2$-$C_6$)-alkynyl, wherein said ($C_1$-$C_6$)-alkyl, O-($C_1$-$C_4$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_0$-$C_6$)-alkylene-COOH, ($C_0$-$C_6$)-alkylene-COO-($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl, O-($C_2$-$C_6$)-alkenyl and ($C_2$-$C_6$)-alkynyl are optionally mono- or polysubstituted by F, Cl or Br;

A is H, F, Cl, Br, OH, $NO_2$, CN, ($C_1$-$C_6$)-alkyl, CO-($C_1$-$C_6$)-alkyl, ($C_1$-$C_6$)-alkylene-COOH, ($C_1$-$C_6$)-alkylene-COO($C_1$-$C_6$)-alkyl, $SO_2$-($C_1$-$C_6$)-alkyl,

$(C_2$-$C_6)$-alkenyl, $(C_2$-$C_6)$-alkynyl, O-$(C_1$-$C_6)$-alkyl, $S(O)_{1-2}$-$(C_1$-$C_6)$-alkyl-, NH-$(C_1$-$C_6)$-alkyl, N-$[(C_1$-$C_6)$-alkyl$]_2$, COO-$(C_1$-$C_6)$-alkyl, $CONH_2$, CONH-$(C_1$-$C_6)$-alkyl, CON-$[(C_1$-$C_6)$-alkyl$]_2$, $SO_2NH_2$, $SO_2$NH-$(C_1$-$C_6)$-alkyl, $SO_2$N-$[(C_1$-$C_6)$-alkyl$]_2$ or NHCOR6, wherein said $(C_1$-$C_6)$-alkyl, CO-$(C_1$-$C_6)$-alkyl, $(C_1$-$C_6)$-alkylene-COOH, $(C_1$-$C_6)$-alkylene-COO$(C_1$-$C_6)$-alkyl, $SO_2$-$(C_1$-$C_6)$-alkyl, $(C_2$-$C_6)$-alkenyl, $(C_2$-$C_6)$-alkynyl, O-$(C_1$-$C_6)$-alkyl, $S(O)_{1-2}$-$(C_1$-$C_6)$-alkyl-, NH-$(C_1$-$C_6)$-alkyl, N-$[(C_1$-$C_6)$-alkyl$]_2$, COO-$(C_1$-$C_6)$-alkyl, CONH-$(C_1$-$C_6)$-alkyl, CON-$[(C_1$-$C_6)$-alkyl$]_2$, $SO_2$NH-$(C_1$-$C_6)$-alkyl and $SO_2$N-$[(C_1$-$C_6)$-alkyl$]_2$ are optionally mono- or polysubstituted by F, Cl, Br, COOH, COO-$(C_1$-$C_6)$-alkyl, $CONH_2$, CONH-$(C_1$-$C_6)$-alkyl, CON$[(C_1$-$C_6)$-alkyl$]_2$ or OCO-$(C_1$-$C_6)$-alkyl;

n is 0, 1, 2 or 3;

R7 and R8 are each independently H, F, Cl, Br, $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl, O-$(C_2$-$C_6)$-alkenyl, O-$(C_2$-$C_6)$-alkynyl, OH, oxo, O-$(C_1$-$C_6)$-alkyl, $NH_2$, NH-$(C_1$-$C_6)$-alkyl, N-$[(C_1$-$C_6)$-alkyl$]_2$, COOH, CO-$(C_1$-$C_6)$-alkyl, COO-$(C_1$-$C_6)$-alkyl, $CONH_2$, CONH-$(C_1$-$C_6)$-alkyl, CON-$[(C_1$-$C_6)$-alkyl$]_2$, $(C_0$-$C_6)$-alkylene-aryl or $(C_1$-$C_6)$-alkylene-COO-$(C_1$-$C_6)$-alkyl, wherein said $(C_1$-$C_6)$-alkyl, O-$(C_1$-$C_6)$-alkyl, O-$(C_2$-$C_6)$-alkenyl, O-$(C_2$-$C_6)$-alkynyl, O-$(C_1$-$C_6)$-alkyl, NH-$(C_1$-$C_6)$-alkyl, N-$[(C_1$-$C_6)$-alkyl$]_2$, CO-$(C_1$-$C_6)$-alkyl, COO-$(C_1$-$C_6)$-alkyl, CONH-$(C_1$-$C_6)$-alkyl, CON-$[(C_1$-$C_6)$-alkyl$]_2$, $(C_0$-$C_6)$-alkylene-aryl and $(C_1$-$C_6)$-alkylene-COO-$(C_1$-$C_6)$-alkyl are optionally substituted by COOH, $CONH_2$, CONH-$(C_1$-$C_6)$-alkyl, CON-$[(C_1$-$C_6)$-alkyl$]_2$, OCO-$(C_1$-$C_6)$-alkyl, F, Cl, $(C_1$-$C_6)$-alkyl or O-$(C_1$-$C_6)$-alkyl; and said R7 and R8 may optionally be bonded together to form a ring fused onto said heterocyclic 4- to 7-membered ring; and

Y is –N=C=O.

16. (New) A compound which is 1-{2-[3-(2-chloro-4,5-difluorobenzoyl)ureido]-4-fluorophenyl}piperidine-4-carboxylic acid and pharmaceutically acceptable salts thereof.